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CITATION:

Satow, Takeshi ...[et al]. Combination of Transcranial Direct Current Stimulation and Neuromuscular Electrical Stimulation Improves Gait Ability in a Patient in Chronic Stage of Stroke. Case Reports in Neurology 2016, 8(1): 39-46

ISSUE DATE:

2016-02

URL:

<http://hdl.handle.net/2433/225086>

RIGHT:

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# Combination of Transcranial Direct Current Stimulation and Neuromuscular Electrical Stimulation Improves Gait Ability in a Patient in Chronic Stage of Stroke

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## Key Words

Transcranial direct current stimulation · Neuromuscular electrical stimulation · Stroke · Gait · Rehabilitation

## Abstract

**Background:** Walking ability is important in stroke patients to maintain daily life. Nevertheless, its improvement is limited with conventional physical therapy in chronic stage. We report the case of a chronic stroke patient showing a remarkable improvement in gait function after a new neurorehabilitation protocol using transcranial direct current stimulation (tDCS) and neuromuscular electrical stimulation (NMES). **Case Presentation:** A 62-year-old male with left putaminal hemorrhage suffered from severe right hemiparesis. He could move by himself with a wheelchair 1 year after the ictus. Anodal tDCS at the vertex (2 mA, 20 min) with NMES at the anterior tibialis muscle had been applied for 3 weeks. The Timed Up and Go test and 10-meter walk test improved after the intervention, which had been maintained for at least 1 month. **Conclusion:** This single case suggests the possibility that tDCS with NMES could be a new rehabilitation approach to improve the gait ability in chronic stroke patients.

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## Introduction

Stroke is a leading cause of life-long disability. Conventional physical, occupational and speech therapies are established means of recovery from such disabilities, which are commonly used in the worldwide rehabilitation settings. However, the recovery of motor function after stroke is usually incomplete. Persistent neurological deficits impair activities of daily living (i.e. dressing, eating, self-care and personal hygiene), which underlie the need for the development of a novel neurorehabilitation approach.

Transcranial direct current stimulation (tDCS) is one of the noninvasive brain stimulation approaches that increasingly gather attention as a means for increasing or decreasing cortical excitability, depending on the delivery of anodal or cathodal stimulation to the cerebral cortex [1]. This method has advantages over other transcranial stimulation techniques, such as its ease of application, the lower cost and more prolonged modulating effect on the cerebral cortex. Although the efficacy of tDCS on hand function and aphasia has been widely evaluated, studies investigating the effects of tDCS on lower limb function have been limited [2–4]. In those studies, only tDCS was used as a neuromodulation method to improve leg function.

It can be assumed that other additional peripheral input might enhance the effect of tDCS and rehabilitation. In fact, tDCS combined with peripheral nerve stimulation improved the motor sequence task with a paretic hand as compared to the two interventions alone [5]. However, studies investigating the improvement of gait ability by the combination of tDCS and peripheral stimulation have never been reported.

Here, we show a patient in chronic stage of hemorrhagic stroke who experienced a surprising improvement in gait ability after the implementation of 3 weeks of combination therapy with tDCS and neuromuscular electrical stimulation (NMES).

## Patient and Method

### Case Presentation

A 62-year-old, right-handed male with a history of hypertension was referred to our hospital for the treatment of left putaminal hemorrhage (fig. 1). On admission, he was stuporous and showed complete hemiparesis on the right side. During the acute period of this hemorrhagic stroke, glyceol was given to control intracranial pressure, and his systolic blood pressure was maintained between 120 and 130 mm Hg with continuous infusion of nicardipine. Without enlargement of the hematoma, he gradually recovered from consciousness disturbance 1 week after the ictus. Conventional rehabilitation including physical, occupational and speech therapies was initiated under cardiorespiratory monitoring. However, deep venous thrombosis occurred, which required anticoagulation and inferior vena cava filter placement. Then, a carcinoma of the kidney was discovered incidentally, and the patient underwent surgical removal of the tumor in the Department of Urology of our hospital. Such treatment prevented him from intensive neurorehabilitation during the acute period and resulted in disuse syndrome. At 4 months after admission, he was readmitted to the Neurosurgery ward to restart rehabilitation.

He was bed-ridden, and his right upper and lower extremities showed contracture. Physical and occupational therapy gradually made him sit and stand, which established his ability to operate a wheelchair by himself at 8 months after admission. Then, he could walk slowly in parallel bars with long leg braces at 1 year after the ictus.

For the further improvement of his gait ability, he underwent a new rehabilitation protocol combining tDCS and NMES.

#### *Transcranial Direct Current Stimulation (tDCS)*

The weak direct current (2 mA) was induced through saline-soaked sponge electrodes (surface 35 cm<sup>2</sup>) and delivered by a specially designed battery-driven, constant current stimulator (DC Stimulator Plus; neuro-Conn GmbH, Ilmenau, Germany). The anode (STIM1) or cathode (STIM2) was positioned above the vertex (Cz) on the international 10/20 electroencephalogram system representing the foot area of the primary sensorimotor cortex (fig. 2a). Its counter electrode was placed over the forehead supraorbital area on the left side (Fp1 on the international 10/20 electroencephalogram system). The stimulation lasted for 20 min each day.

#### *Neuromuscular Electrical Stimulation*

Commercially available NMES was delivered to the anterior tibialis muscle on the right with Auto TENS Pro (Homer Ion Co. Ltd., Tokyo, Japan). The intensity of stimulation was 40% of the maximum output (the theoretical maximum output was reported to be 46 mA, but the actual intensity delivered is dependent on the skin resistance), which did not induce pain or discomfort in the patient. The stimulator current waveform was the original exponential tapering waveform and designed to produce co-contractions in the lower extremity muscle groups at a frequency of 50 Hz with a pulse width of 110  $\mu$ s. The duty cycle was a 5-second stimulation with a 1-second pause for a period of 20 min. Impulses were delivered through two silicon-rubber electrodes on the shin in order to facilitate correcting his equinus foot.

#### *Short-Term Effects of tDCS (Pretreatment Session for Parameter Customization)*

Before the treatment period, the anode or cathode of the tDCS was centered at Cz (international 10–20 system), and the 10-meter walk test (10 MWT) and Timed Up and Go test (TUG) were carried out during stimulation. The results of those tests were compared with those achieved without stimulation. We intended to employ the stimulation protocol in which the results were better.

#### *Combined tDCS and NMES (Treatment Session)*

The patient underwent tDCS and NMES for 20 min 5 days a week for a treatment period of 3 weeks (fig. 2b).

#### *Evaluation of Gait Ability and Cognitive Function*

Before and after the treatment period, gait and cognitive function were evaluated by physical and speech therapists. This evaluation was also carried out 1.5 weeks after the beginning of the intervention and 1 month after the end of the intervention.

To measure the walking abilities, the TUG test and 10 MWT were used. The shorter the time to conduct TUG and 10 MWT, the better the ability of gait is.

With regard to the evaluation of cognitive function, neuropsychological batteries, such as the Mini-Mental State Examination, Raven's Colored Progressive Matrices, Trail Making test and Word Fluency test, were measured before and after the intervention.

## Results

The patient did not report any complication related to tDCS and NMES. Subjective rating for satisfaction with this treatment scored 100 (0 = very unsatisfactory, 100 = very satisfactory).

In the pretreatment session, the patients' gait ability was better during cathodal stimulation at Cz. TUG without stimulation was 42.6 s. However, TUG with anodal or cathodal stimulation at Cz was 44.1 or 35.0 s, respectively. 10 MWT without stimulation took 44.0 s. The 10 MWT with anodal or cathodal stimulation was 44.0 and 38.5 s, respectively. He also reported that he could walk with ease during cathodal stimulation. On the other hand, when anodal stimulation was applied, he reported that his leg on the right side was heavy. Thus, we decided to use cathodal stimulation at Cz as the intervention pattern for the treatment session.

The results of TUG and 10 MWT are shown in [figure 3a](#) and [b](#), respectively. TUG before the intervention was 42.6 s. TUG 1.5 weeks after and at the end of the intervention were 30.1 s and 28.1 s, respectively. This improvement was maintained 1 month after the intervention (27.7 s). 10 MWT before the intervention was 44.0 s. 10 MWT 1.5 week after and at the end of the intervention were 36.8 and 30.5 s, respectively. 10 MWT 1 month after the intervention was 34.1 s. Cognitive function did not change after tDCS and NMES, as shown in [table 1](#).

## Discussion

In the present case report, we showed a chronic stroke patient who underwent tDCS and NMES and showed a surprising improvement in gait ability. This improvement was maintained at least for 1 month after the intervention.

### *Neuromodulation Therapy in Rehabilitation*

Conventional neurorehabilitation often results in the incomplete recovery of motor function after stroke. With regard to walking function, further improvement should not be expected later than 11 weeks after stroke, even with administration of rehabilitation [\[6\]](#). Therefore, it is difficult to say whether the gait function in the present patient is due to conventional rehabilitation and/or natural course.

Noninvasive brain stimulation is an emerging neuromodulation method to induce brain plasticity. Among such methods, TMS and tDCS are most commonly used in the field of basic neuroscience and clinical application. Since tDCS is not directly associated with the neural firings and has a minimal risk of seizures, tDCS is safer than TMS for clinical application. It has been shown that tDCS can modulate motor cortical excitability for a period of time that outlasts the stimulation window [\[7\]](#). Not only neurophysiological modulation but also improvement in motor outcome in stroke rehabilitation has been reported in tDCS studies.

### *The Role of NMES in Motor Recovery*

A recent animal study using mice showed that the DCS with repetitive low-frequency synaptic activation is effective in inducing motor plasticity, which is mediated by a long-lasting synaptic potentiation mediated by *BDNF* [\[8\]](#). As reported by Thibaut et al. [\[9\]](#), the response to tDCS in patients with consciousness disturbance might be influenced by grey matter preservation and residual metabolic activity of the cortical and subcortical area, as measured by structural MRI and positron emission tomography. It is important to select appropriate patients who will respond to tDCS (tDCS responders) by using noninvasive neuroimaging.

Results of clinical studies also showed that the application of tDCS on the motor cortex in combination with physical and occupational therapy improves motor outcome after stroke [10]. It is conceivable that peripheral input can enhance and facilitate the cortical plasticity. Celnik et al. [5] reported the effect of the combination of peripheral nerve stimulation (PNS) and tDCS on finger motor sequence task in chronic stroke patients. Peripheral electrical stimulation might have an additional effect on the plastic change in the motor cortex induced by tDCS.

#### *The Effect of tDCS on Gait Ability*

In the present article, cathodal tDCS improved the gait ability, which was different from the report by Sohn et al. [4] showing that anodal stimulation by tDCS improved the balance and strength of the affected lower extremity. This difference might be due to interindividual variability observed in tDCS studies [11]. Based on this interindividual variability, we conducted the pretreatment session to determine and confirm the appropriate stimulation parameters in this particular patient (parameter customization). Previous studies could demonstrate the improvement of only neurophysiological parameters, which are related to gait function [2, 3]. This is the first case report that showed an apparent improvement in walking ability, i.e. gait speed.

#### *Limitation of this Study*

This study investigated a single case, and we did not conduct any comparison with sham stimulation. In the present single case study, using a combination of two modalities, we can conclude neither the efficiency of one of the treatments nor the effect of the combined treatment of the placebo effect of the additional treatment. Further study is needed to clarify this problem.

However, we believe that it is unlikely because its effect was immediate in spite of the fact that the patient was incapable of walking without assistance even 1 year after the onset of hemorrhagic stroke. In addition, there was a clear polarity-dependent effect in the pretreatment session, without any knowledge about the tDCS parameter.

Another concern is the location of the stimulated site by tDCS, i.e. Cz on the international 10/20 electroencephalogram system. Cz is situated at the midpoint between the nasion and inion along the midsagittal line. Since the tDCS electrode is relatively large (35 cm<sup>2</sup>), it is conceivable that the cerebral cortex around Cz was stimulated on both sides in the present study. Thus, it is possible that both sides of the foot area of the primary sensorimotor cortex or even medial frontal areas including supplementary motor areas were influenced by tDCS. Now we are investigating the effect of tDCS delivered to each side of the foot area of the primary sensorimotor area on gait ability in chronic stroke patients.

### **Conclusion**

This case report raises the possibility that only 3 weeks of tDCS and NMES combination therapy improves the gait abilities in chronic stroke patients. This novel rehabilitation strategy might become a promising supplementary choice for the improvement in gait function in stroke patients seeking rehabilitation.



## Acknowledgments

This study was partly supported by a Grant-in-Aid for Scientific Research (15H03044), a Grant-in-Aid for Scientific Research on Innovative Areas (15H05880, 15H05871) from the Japan Society for the Promotion of Science, STEP2 (27280201) and 2736040 from the Japan Agency for Medical Research and Development, AMED, and the Research Grant (2015) from the Brain Science Foundation (to T.M.).

## Statement of Ethics

The patient gave written informed consent before the study, and the Institutional Review Board of Nagahama City Hospital approved this study.

## Disclosure Statement

All authors declare that they have no conflicts of interest.

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**Table 1.** Results of cognitive function before (Pre) and after (Post) the intervention

	Pre	Post
MMSE (/30)	27	27
RCPM (/36)	26	27
TMT, s		
Part A	47	48
Part B	132	130
WFT, words		
Semantic	9	8
Phonemic	6	6

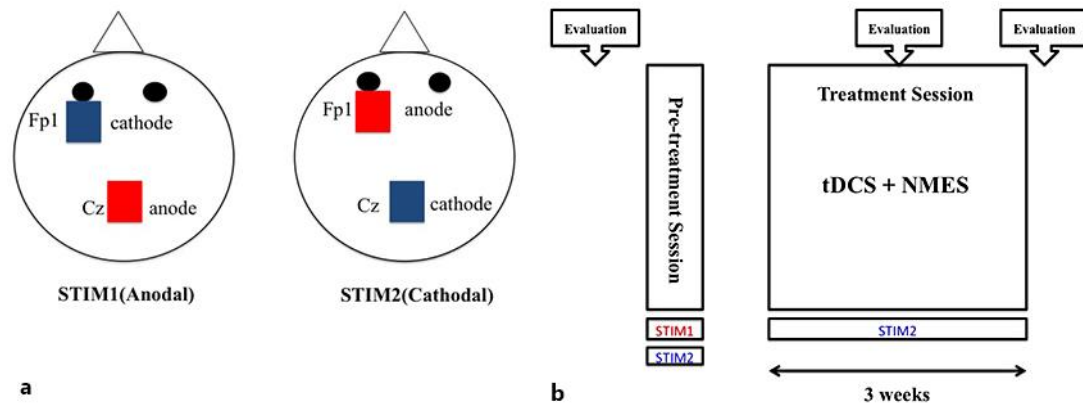
MMSE = Mini-Mental State Examination; RCPM = Raven's Colored Progressive Matrices; TMT = Trail Making test; WFT = Word Fluency test.



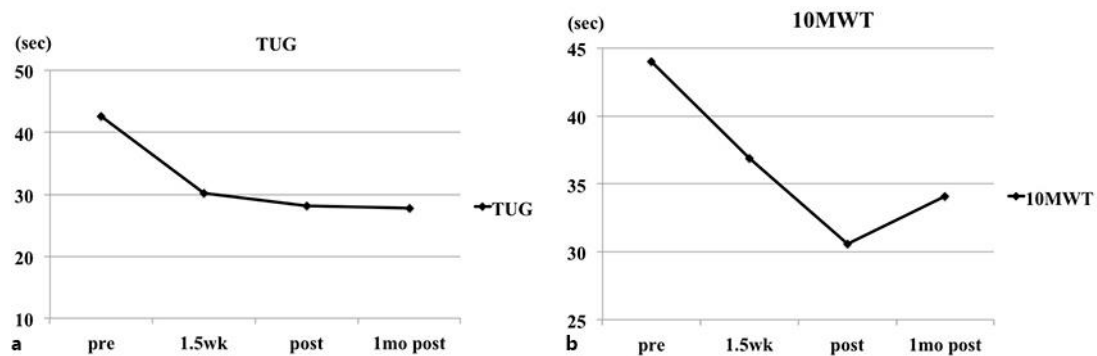
**Fig. 1.** CT of the brain on admission, showing left putaminal hemorrhage.



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**Fig. 2.** **a** Stimulation pattern of tDCS in the present study. STIM1 indicates that the anode was placed on the Cz and the cathode on the forehead. STIM2 was its opposite polarity. **b** Time course of the intervention in the present patients. Before the intervention (pretreatment session), the pattern of intervention (STIM1 or STIM2) that was more beneficial to his gait ability was evaluated. His gait ability was better in STIM2, so this stimulation had been applied in the treatment sessions for 3 weeks.



**Fig. 3.** Time course of the results of the TUG test (**a**) and 10 MWT (**b**) before and after the intervention. Pre = before the intervention; 1.5wk = 1.5 weeks after the start of the intervention; post = at the end of the intervention; 1mo post = 1 month after the end of the intervention.